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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,225	03/17/2006	Ashfaq Mahmood	58345(70207)	5276
21874 7590 02/01/2011 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
RIDER, LANCE W				
ART UNIT		PAPER NUMBER		
1618				
MAIL DATE		DELIVERY MODE		
02/01/2011		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/534,225

**Applicant(s)**

MAHMOOD ET AL.

**Examiner**

LANCE RIDER

**Art Unit**

1618

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 18 November 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16-21, 29-32, 36, 40-43, 46-48, 54, 63-65 and 69 is/are pending in the application.
- 4a) Of the above claim(s) 20, 21, 31, 36, 40-43, 46-48, 54, 63-65 and 69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-19, 29, 30 and 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-552)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 11/19/2010
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### **Status of the Application**

The remarks and amendments filed on November 18<sup>th</sup> 2010 are acknowledged. Claims 29, 31, and 32 are amended, claims 1-15, 22-24, 33-35, 37-39, 44-45, 49-53, 55-62, 66-68 are canceled, claims 16-21, 29-32, 36, 40-43, 46-48, 54, 63-65 and 69 are pending, claims 20-21, 31, 36, 40-43, 46-48, 54, 63-65 and 69 are withdrawn.

### **Response to arguments**

## **Maintained Rejections**

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

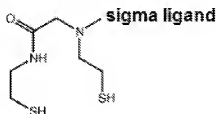
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 16-19, 29-30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over John et al., U.S. Patent 5,919,934 in view of Largent, B. L., (The American Society for Pharmacology and Experimental Therapeutics, 1987).**

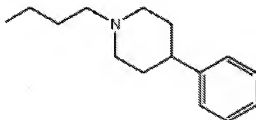
This rejection is MAINTAINED for the reasons of record set forth in the office action mailed on November 18<sup>th</sup> 2010 and for the reasons set forth below. Applicant's arguments have been fully considered but they are not persuasive.

Applicant's argue: "one of ordinary skill in the art could not be motivated to modify these specific compounds of John by "replacement of the piperidine disclosed by John" with "the 4-phenylpiperidine of Largent" to arrive at the presently-claimed compounds and complexes; such a combination would not result in the presently-claimed compounds and complexes."

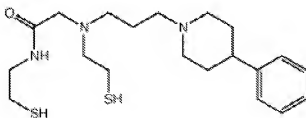
As previously stated John teaches sigma receptor ligands connected to the metal chelator (below). John teaches that connecting this chelator to the sigma receptor ligands allows for imaging sigma receptors.



Largent teaches that n-propyl-4-phenylpiperidine is a good sigma receptor ligand.



Attaching sigma ligand n-propyl-4-phenylpiperidine to the imaging chelator of John would indeed lead to the instantly elected species shown below.



Regarding the linker groups applicant refers too in John. As previously stated John teaches that the linker between the metal chelators and the sigma receptor ligands

(piperidine) can be varied and include linkers of  $\text{CH}_2\text{-N-CH}_2$ , the identical length of applicants claimed linker (a propyl chain), and present in the n-propyl-4-phenylpiperidine sigma receptor ligand of Largent.

Applicant also argues against the predictability of this combination.

John teaches metal chelators attached to sigma receptor ligands can be used at visualization agents for such receptors. These ligands require a sigma receptor ligand with a piperidine core linker to a metal chelator. Largent teaches that n-propyl-4-phenylpiperidine is a useful sigma receptor ligand. Largent also teaches that extension of the alkyl chain at the 4 position of the phenylpiperidine increases the binding affinity of 4-phenylpiperidine ligands significantly from 2800 nm for just a methyl to 15 nm of a propyl group. The skilled artisan would have thus expected that extensions at this position would not prevent binding of the sigma ligand to the receptor, conversely they would likely enhance binding. Thus the artisan would have expected that the metal chelator tagged sigma ligand would bind tightly to the receptor and given the inherent visibility of the metal allow detection of the agent.

Applicant also argues that the claimed compounds in claims 20, 21, and 31 are not 4-phenylpiperidine containing complexes, the elected species.

As applicant's have pointed out claims 20, 21, and 31 do not encompass the elected species and these claims are hereby withdrawn.

### **Conclusion**

No claims allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LANCE RIDER whose telephone number is (571)270-1337. The examiner can normally be reached on M-F 11-12 and 1-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LANCE RIDER/  
Examiner, Art Unit 1618

/Jake M. Vu/  
Primary Examiner, Art Unit 1618